```
=> d his

     (FILE 'HOME' ENTERED AT 14:28:24 ON 19 MAY 2004)

     FILE 'REGISTRY' ENTERED AT 14:28:43 ON 19 MAY 2004
L1             6 S T[RED]LT[RED][EDATSQ][RED]GLK/SQSP

     FILE 'CAPLUS, USPATFULL' ENTERED AT 14:29:10 ON 19 MAY 2004
L2             4 S L1
L3             4 DUP REM L2 (0 DUPLICATES REMOVED)

     FILE 'REGISTRY' ENTERED AT 14:29:27 ON 19 MAY 2004
L4             3 S TRLTRRGLK/SQSP OR TRLTKRGLK/SQSP OR TRLTRKGLK/SQSP
L5             1 S TRLTREKRGLK/SQSP
L6             3 S TRLTRKERGLK/SQSP OR TRLTRDKRGLK/SQSP OR TRLTRKDRGLK/SQSP
L7             7 S L4 OR L5 OR L6

     FILE 'CAPLUS, USPATFULL' ENTERED AT 14:31:24 ON 19 MAY 2004
L8             4 S L7
```

```
=> s (hormone replacement?) or hormone replenishment?
L1        5704 (HORMONE REPLACEMENT?) OR HORMONE REPLENISHMENT?

=> s l1(P)(HGH or human growth hormone or samatostatin)
L2          44 L1(P)(HGH OR HUMAN GROWTH HORMONE OR SAMATOSTATIN)

=> d bib, hit

L2   ANSWER 1 OF 44  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:323635  CAPLUS
DN   140:315407
TI   Long-term improvement of quality of life during growth hormone (GH)
     replacement therapy in adults with GH deficiency, as measured by questions
     on life satisfaction-hypopituitarism (QLS-H)
AU   Rosilio, Myriam; Blum, Werner F.; Edwards, David J.; Shavrikova, Elena P.;
     Valle, Domenico; Lamberts, Steven W. J.; Erfurth, Eva Marie; Webb, Susan
     M.; Ross, Richard J.; Chihara, Kazuo; Henrich, Gerhard; Herschbach, Peter;
     Attanasio, Andrea F.
CS   Lilly Research Laboratories, Eli Lilly and Co., Indianapolis, IN, 46285,
     USA
SO   Journal of Clinical Endocrinology and Metabolism (2004), 89(4), 1684-1693
     CODEN: JCEMAZ; ISSN: 0021-972X
PB   Endocrine Society
DT   Journal
LA   English
RE.CNT  38    THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT   Antidepressants
     Body, anatomical
       Human
     Sex
        (growth hormone replacement therapy in
        adults with GH deficiency)


=> dup rem l2
PROCESSING COMPLETED FOR L2
L3          44 DUP REM L2 (0 DUPLICATES REMOVED)

=> d bib, hit 20-
YOU HAVE REQUESTED DATA FROM 25 ANSWERS - CONTINUE? Y/(N):y


L3   ANSWER 20 OF 44  WPIDS  COPYRIGHT 2004 THOMSON DERWENT on STN
AN   2001-564579 [63]   WPIDS
CR   2001-225871 [15]
DNC  C2001-167532
TI   Treatment for a patient with symptoms consistent with multiple sclerosis
     involves administering human growth hormone.
DC   B04
IN   CHEIN, E Y M
PA   (CHEI-I) CHEIN E Y M
CYC  1
PI   US 2001012832   A1 20010809 (200163)*      15
ADT  US 2001012832 A1 Div ex US 1999-385133 19990825, US 2001-782015 20010212
FDT  US 2001012832 A1 Div ex US 6187750
PRAI US 1999-385133       19990825; US 2001-782015       20010212
AB   US2001012832 A UPAB: 20011031
     NOVELTY - Treating a human subject having symptoms consistent with
     multiple sclerosis (MS) comprises administering a regimen of doses of
     human growth hormone (HGH) (less
```

than 0.5 mg/day).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a kit for treating the symptoms associated with MS comprising **HGH** and at least one supplemental hormone selected from sex hormone (preferably testosterone, progesterone or estrogen), melatonin hormone, adrenal hormone, thyroid hormone, or thymus hormone. The kit is for establishing a regimen for the replenishment of **HGH** and the supplemental growth hormone to predetermine physiological levels.; and

(2) a method for replenishing **HGH** to it's original level comprising measuring a sample a blood to determine the level of **HGH** then adding more **HGH**.

ACTIVITY - Neuroprotective; Antiinflammatory.

A 43 year old male, suffering from white matter signal abnormalities and subtle diffuse signal abnormalities consistent with multiple sclerosis (detected in the first exam in 1995 by brain magnetic resonance image (MRI)), was placed on a **hormone replenishment** regiment, by administering **human growth hormone** (**HGH**) in an amount of 0.5 mg/dose twice daily subcutaneously. The patient was also administered with testosterone, melatonin, dehydroepiandrosterone (DHEA), thyroid, pregnenolone and thymus hormones. An examination later in 1998 showed a significant diminishment of lesions, including the actual disappearance of lesions from the magnetic resonance imaging (MRI) scan. The previously rioted large left middle cerebrallar peduncle lesion was very subtle on the current film that was initially interpreted as normal. A small lesion in the anterior limb of the internal capsule seen in 1995, could not be visualized. A right posterior frontal deep white matter lesion was slightly smaller compared to that previously noted in 1995. The remaining lesions noted in the 1995 examination remained unchanged. Brain evoked response studies also indicated improvement in speed of neurotransmission after the treatment. The visual evoked responses revealed optic nerve involvement by multiple sclerosis. Studies of the patient's visual evoked responses before and after **hormone replenishment** therapy indicated improvement in the optic nerve. The patient also regained complete motor strength and sensory disturbances disappeared.

USE - For treatment of multiple sclerosis (claimed).

ADVANTAGE - The **HGH** is administered in low dose-high frequency manner that mimic the natural rhythm of the body of secretion of **HGH** by pituitary gland. This avoids the adverse side effects associated with the intermittent administration of higher pharmacological doses e.g. for 3 days per week, as that of the prior art.

Dwg.0/9

L3 ANSWER 21 OF 44 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 2001-225871 [23] WPIDS
CR 2001-564579 [63]
DNC C2001-067377
TI Treating multiple sclerosis symptoms by administering human growth hormone at a dose of less than 0.5 mg per day and also, optionally, replenishing melatonin, thymus, thyroid, adrenal and/or sex hormones to predetermined levels.
DC B04
IN CHEIN, E Y M
PA (CHIE-I) CHIEN E Y M; (EVER-N) EVERYOUNG TECHNOLOGIES INC
CYC 2
PI US 6187750 B1 20010213 (200123)* 17
JP 2002154982 A 20020528 (200250)# 45
ADT US 6187750 B1 US 1999-385133 19990825; JP 2002154982 A JP 2000-382920 20001110
PRAI US 1999-385133 19990825; JP 2000-382920 20001110
AB US 6187750 B UPAB: 20020807
NOVELTY - Treating and reducing the symptoms of multiple sclerosis

comprises administering **human growth hormone** (**HGH**) at a dose of less than 0.5 mg per day.

ACTIVITY - Antiinflammatory; neuroprotective.

The MRI scan of a 43 year old male in 1995 revealed multiple white matter signal abnormalities, as well as subtle diffuse signal abnormalities consistent with MS. Soon after this test the patient was placed on a **hormone replenishment** regimen, featuring twice daily subcutaneous doses of 0.5 mg of **human growth hormone**. Testosterone, melatonin, DHEA (not defined), thyroid, pregnenolone and thymus hormone were also given in order to bring the levels of these hormones up the normal levels of a human male. A later examination in 1998 noted significant diminishment of the lesions, including the actual disappearance from the MRI scan of some lesions. Brain evoked response studies also indicated improvement in speed of neurotransmission after the treatment. For example, visual evoked responses may reveal optic nerve involvement by MS. Studies of the patient's visual evoked responses before and after **hormone replenishment** therapy revealed faster conduction speed after the therapy, indicating improvement in the optic nerve. The patient also regained complete motor strength and sensory disturbances disappeared.

MECHANISM OF ACTION - Insulin-like growth factor hormones, (IGF) may promote myelin regeneration, reducing and sometimes eliminating inflammatory lesions.

USE - The treatment methods reduce the symptoms associated with multiple sclerosis.

ADVANTAGE - The administration of frequent lower doses of **HGH** mimics the natural rhythm of the body, thus the patient should experience none of the adverse side effects associated with higher and more intermittent pharmacological doses of **HGH**.

Dwg.0/9

L3 ANSWER 22 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:310646 CAPLUS
DN 136:380410
TI Commencing growth hormone replacement in adults with a fixed low dose. Effects on serum lipoproteins, glucose metabolism, body composition, and cardiovascular function
AU Gillberg, P.; Bramnert, M.; Thoren, M.; Werner, S.; Johannsson, G.
CS Department of Medical Sciences, University Hospital, Uppsala, Swed.
SO Growth Hormone & IGF Research (2001), 11(5), 273-281
CODEN: GHIRF9; ISSN: 1096-6374
PB Churchill Livingstone
DT Journal
LA English
RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT Cardiovascular system
Exercise
Human
(**growth hormone replacement** in adults with a fixed low dose. effects on serum lipoproteins, glucose metabolism, body composition, and cardiovascular function)

L3 ANSWER 23 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:624357 CAPLUS
DN 132:18985
TI Estrogen replacement therapy and the response to human growth hormone
AU Ceda, Gian Paolo; Valenti, Giorgio; Hoffman, Andrew R.
CS University of Parma, Parma, Italy
SO Sex-Steroid Interactions with Growth Hormone, [Proceedings of the International Symposium on Sex-Steroid Interactions with Growth Hormone], Naples, Fla., Oct. 22-25, 1998 (1999), Meeting Date 1998, 202-208.

Editor(s): Veldhuis, Johannes D.; Giustina, Andrea. Publisher: Springer, New York, N. Y.
CODEN: 68FEAX
DT Conference
LA English
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT **Hormone replacement** therapy
(*estrogen replacement therapy and the response to* **human growth hormone**)

L3 ANSWER 24 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:154188 CAPLUS
DN 130:307088
TI Apo E phenotype and changes in serum lipids in adult patients during growth hormone replacement
AU Leese, G. P.; Wallymahmed, M.; Wieringa, G.; VanHeyningen, C.; MacFarlane, I. A.
CS Department of Endocrinology, Ninewells Hospital, Dundee, UK
SO European Journal of Endocrinology (1999), 140(2), 174-179
CODEN: EJOEEP; ISSN: 0804-4643
PB BioScientifica
DT Journal
LA English
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
AB To determine whether apo E phenotype influences changes in lipid profiles induced by growth **hormone replacement** in growth *hormone (GH)-deficient adults. Patients were treated for 6 mo with recombinant human GH (***hGH***), given in a dose of 0.125 U/kg per wk for 4 wk followed by 0.25 U/kg per wk thereafter. The effects on serum lipids and the influence of apo E phenotype were examined Thirty patients (aged 35.1 yr; mean) with adult growth hormone deficiency were included in the study. Fasting serum samples were analyzed for apo E phenotype total cholesterol, high-d. lipoprotein (HDL)-cholesterol, triglycerides, lipoprotein (a) (Lp(a)) and IGF-1. Low-d. lipoprotein (LDL)-cholesterol was calculated using the Friedwald formula. Six months of replacement treatment with* **hGH** *resulted in a reduction in HDL-cholesterol from* 0.90 to 0.68 mmol/L, and a small, nonsignificant reduction in total cholesterol from 6.14 to 5.99 mmol/L. There was no significant change in the other lipid parameters. The decrease in HDL-cholesterol concentration was greater in patients carrying the apo E2 allele (0.40 mmol/L) than in patients homozygous for the apo E3 allele (0.23 mmol/L) and patients carrying the apo E4 allele (0.15 mmol/L). Patients with the apo E4 allele had lower baseline cholesterol concns. than patients lacking the apo E4 allele, and this persisted after treatment with **hGH**. Apo E phenotype may be a determining factor in the response of HDL-cholesterol to **hGH** in GH-deficient adults.

L3 ANSWER 25 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:728296 CAPLUS
DN 130:33495
TI All hormone replacement therapy
IN Chein, Edmund Y. M.
PA USA
SO Jpn. Kokai Tokkyo Koho, 69 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI JP 10298103 A2 19981110 JP 1997-369889 19971215
US 5855920 A 19990105 US 1996-766320 19961213
GB 2320190 A1 19980617 GB 1997-15349 19970721
GB 2320190 B2 20010815
SG 78281 A1 20010220 SG 1997-4407 19971211
CN 1233503 A 19991103 CN 1998-101688 19980430
HK 1009402 A1 20011130 HK 1998-110466 19980904
PRAI US 1996-766320 A 19961213
AB **Hormone replacement** therapy is used for restoration or balance of a select group of hormones to maintain optimal physiol. level and to improve health and average life expectancy. The **hormone replacement** therapy involves human growth hormones, sex hormones, pineal gland hormones, adrenal hormones, thyroid hormones, and thymus hormones. Composition containing **human growth hormone**, free testosterone, progesterone, estrogen, melatonin, DHEA, thyroid hormone, pregnenolone, and thymus hormone was prepared and used.
IT 53-43-0, DHEA 57-83-0, Progesterone, biological studies 58-22-0, Testosterone 73-31-4, Melatonin 145-13-1, Pregnenolone 12629-01-5, **Human growth hormone**
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**hormone replacement** therapy involves human growth hormones, sex hormones, pineal gland hormones, adrenal hormones, thyroid hormones, and thymus hormones for improving health and life expectancy)

L3 ANSWER 26 OF 44 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1998-289306 [26] WPIDS
DNC C1998-089642
TI **Hormone replenishment** method for improvement of life expectancy - comprises evaluation of blood levels of **hGH** and several other hormones, then establishing regime to achieve optimum levels.
DC B01 B04
IN CHEIN, E Y M
PA (CHEI-I) CHEIN E Y M; (CHEI-I) CHEIN E
CYC 6
PI GB 2320190 A 19980617 (199826)* 49
JP 10298103 A 19981110 (199904) 69
US 5855920 A 19990105 (199909)
KR 98064080 A 19981007 (199949)
CN 1233503 A 19991103 (200011)#
SG 78281 A1 20010220 (200117)
GB 2320190 B 20010815 (200147)
ADT GB 2320190 A GB 1997-15349 19970721; JP 10298103 A JP 1997-369889 19971215; US 5855920 A US 1996-766320 19961213; KR 98064080 A KR 1997-68149 19971212; CN 1233503 A CN 1998-101688 19980430; SG 78281 A1 SG 1997-4407 19971211; GB 2320190 B GB 1997-15349 19970721
PRAI US 1996-766320 19961213; CN 1998-101688 19980430
TI **Hormone replenishment** method for improvement of life expectancy - comprises evaluation of blood levels of **hGH** and several other hormones, then establishing regime to achieve optimum levels.
AB GB 2320190 A UPAB: 19980701
A **hormone replenishment** method comprises : (a) determining that the level of **human growth hormone** (**hGH**) and at least two supplemental hormones selected from sex hormone, melatonin hormone, adrenal hormone, thyroid hormone and thymus hormone are below optimal levels; and (b) establishing a regime with suitable amounts of the deficient hormones to give optimal levels. Also claimed is a kit containing **hGH** and at least two of the above hormones.

USE - The method increases life expectancy and life span (claimed) by reversal and prevention of the symptoms of aging.

ADVANTAGE - Combined therapy avoids the side effects (fluid retention, carpal tunnel syndrome) which may be associated with previous methods of **hGH** administration, because the low dose-high frequency regime mimics the body's own release of hormones.

Dwg.0/8

L3 ANSWER 27 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:706677 CAPLUS
DN 136:129104
TI Growth hormone replacement in young adults: if and when to continue?
AU Johnston, D. G.; Al-Shoumer, K. A. S.; Beshyah, S. A.; Chrisoulidou, A.; Kousta, E.; Anyaoku, V.
CS Unit of Metabolic Medicine, Imperial College School of Medicine, St Mary's Hospital, London, UK
SO Adolescent Endocrinology (1998), 17-23. Editor(s): Stanhope, Richard. Publisher: BioScientifica Ltd., Bristol, UK.
CODEN: 69BVXQ
DT Conference; General Review
LA English
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT Blood vessel, disease
Human
(**growth hormone replacement** in young adults)

L3 ANSWER 28 OF 44 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
AN 1997-079182 [08] WPIDS
DNC C1997-025459
TI Medicaments containing 20 kD **human growth hormone** - useful for **hormone replacement** therapy and to stimulate lipolysis e.g. for improving body compsn..
DC B04 D16
IN ASADA, N; HONJO, M; HORIKOMI, K; IKEDA, M; KAMIOKA, T
PA (MITK) MITSUI TOATSU CHEM INC; (SCHD) SCHERING AG
CYC 18
PI EP 753307 A2 19970115 (199708)* EN 19
R: AT BE CH DE DK FI FR GB IT LI NL SE
AU 9656255 A 19970116 (199711)
AU 680792 B 19970807 (199740)
JP 09216832 A 19970819 (199743) 10
KR 97000242 A 19970121 (199801)
NZ 286884 A 19971219 (199807)
CN 1145808 A 19970326 (200106)
US 6399565 B1 20020604 (200242)
ADT EP 753307 A2 EP 1996-304855 19960701; AU 9656255 A AU 1996-56255 19960628; AU 680792 B AU 1996-56255 19960628; JP 09216832 A JP 1996-138413 19960531; KR 97000242 A KR 1996-25703 19960629; NZ 286884 A NZ 1996-286884 19960625; CN 1145808 A CN 1996-110983 19960629; US 6399565 B1 Div ex US 1996-668469 19960625, US 1997-990774 19971215
FDT AU 680792 B Previous Publ. AU 9656255
PRAI JP 1995-316883 19951205; JP 1995-163572 19950629
TI Medicaments containing 20 kD **human growth hormone** - useful for **hormone replacement** therapy and to stimulate lipolysis e.g. for improving body compsn..
AB EP 753307 A UPAB: 19970909
Medicinal compsns. comprising an authentic 20 kD **human growth hormone** (**hGH**) and a carrier or diluent are new.

USE - The polypeptides can be used for growth **hormone**

replacement therapy in adults, especially **hGH**-deficient adults, to improve body compsn., stimulate lipolysis and/or increase serum IGF-1 levels (claimed).

ADVANTAGE - The 20 kD **hGH** has less tendency to induce glucose intolerance than the known 22 kD **hGH**.

Dwg.0/6

L3 ANSWER 29 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:806644 CAPLUS
DN 128:97913
TI The effect of recombinant human GH replacement therapy on lipoprotein(a) and other lipid parameters in adults with acquired GH deficiency: results of a double-blind and placebo-controlled trial
AU Nolte, Wilhelm; Radisch, Carsten; Armstrong, Victor; Hufner, Michael; von zur Muhlen, Alexander
CS Department Gastroenterology and Endocrinology, Georg-August-University, Gottingen, D-37075, Germany
SO European Journal of Endocrinology (1997), 137(5), 459-466
CODEN: EJOEEP; ISSN: 0804-4643
PB BioScientifica
DT Journal
LA English
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Lipoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Lp(a); recombinant **human growth hormone** **replacement** therapy effect on lipoprotein (a) and other lipid parameters in adults with acquired growth hormone deficiency)

IT Glycerides, biological studies
Lipids, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(blood; recombinant **human growth hormone** **replacement** therapy effect on lipoprotein (a) and other lipid parameters in adults with acquired growth hormone deficiency)

IT Lipoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(high-d.; recombinant **human growth hormone** **replacement** therapy effect on lipoprotein (a) and other lipid parameters in adults with acquired growth hormone deficiency)

IT Lipoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(low-d.; recombinant **human growth hormone** **replacement** therapy effect on lipoprotein (a) and other lipid parameters in adults with acquired growth hormone deficiency)

IT Glycerides, biological studies
Lipoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(recombinant **human growth hormone** **replacement** therapy effect on lipoprotein (a) and other lipid parameters in adults with acquired growth hormone deficiency)

IT 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(blood; recombinant **human growth hormone** **replacement** therapy effect on lipoprotein (a) and other lipid parameters in adults with acquired growth hormone deficiency)

IT 9002-72-6, Somatotropin
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(deficiency; recombinant **human growth hormone replacement** therapy effect on lipoprotein (a) and other lipid parameters in adults with acquired growth hormone deficiency)

IT 9002-72-6, Growth hormone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(recombinant **human growth hormone replacement** therapy effect on lipoprotein (a) and other lipid parameters in adults with acquired growth hormone deficiency)

IT 57-88-5, Cholesterol, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(recombinant **human growth hormone replacement** therapy effect on lipoprotein (a) and other lipid parameters in adults with acquired growth hormone deficiency)

L3 ANSWER 30 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:589691 CAPLUS
DN 125:266298
TI Superoxide anion release from neutrophils in growth hormone deficient adults before and after replacement therapy with recombinant human growth hormone
AU Reinisch, N.; Schratzberger, P.; Finkenstedt, G.; Kaehler, C. M.; Wiedermann, C. J.
CS Department Internal Medicine, University Innsbruck, Innsbruck, A-6020, Austria
SO Naunyn-Schmiedeberg's Archives of Pharmacology (1996), 354(3), 369-373
CODEN: NSAPCC; ISSN: 0028-1298
PB Springer
DT Journal
LA English
AB The observations that growth hormone primes neutrophils and stimulates various activities of monocytes suggested that it plays a role in the regulation of leukocyte biol. The in vivo reduction of growth hormone levels may be responsible for the functional impairment of leukocytes observed in growth hormone deficient children. Whether leukocyte function is impaired in growth hormone deficient adults is not known as yet. The authors therefore studied superoxide anion release from neutrophils and chemotaxis of monocytes in 15 patients with adult-onset growth hormone deficiency before and after a period of 6 mo of replacement therapy with recombinant **human growth hormone**. Analyses were performed by comparing functions of the leukocytes from these patients with those from age and sex-matched healthy control subjects. Before growth hormone treatment, patients received appropriate replacement therapy with thyroid, adrenal and gonadal hormones. The dose of recombinant **human growth hormone** was 0.25-0.5 U/kg/wk (0.013-0.026 mg/kg/day) throughout the whole period of replacement therapy. In growth hormone deficient subjects, formylpeptide-triggered release of superoxide anions from neutrophils was significantly suppressed by about 40% before treatment as compared to healthy control subjects. After 6 mo of replacement therapy, neutrophil superoxide anion release was similar in patients and healthy individuals. Neither before nor after replacement therapy, however, was there a difference in monocyte migration between control and growth hormone deficient subjects. These data indicate that neutrophil function is somehow altered in growth hormone deficient patients, even when receiving appropriate therapy with thyroid, adrenal and gonadal hormones, but that neutrophil function can be restored to near normalcy by growth **hormone replacement** therapy. This

would suggest that suppressed neutrophil respiratory burst is due to the deficiency in growth hormone.

L3 ANSWER 31 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:351029 CAPLUS
DN 125:49363
TI Growth hormone deficiency in adults: Characteristics and response to growth hormone replacement
AU Lieberman, Steven A.; Hoffman, Andrew R.
CS Department Internal Medicine, University Texas Medical Branch, Galveston, TX, 77555-1060, USA
SO Journal of Pediatrics (St. Louis) (1996), 128(5, Pt. 2), S58-S60
CODEN: JOPDAB; ISSN: 0022-3476
PB Mosby-Year Book
DT Journal; General Review
LA English
AB A review with 20 refs. Despite adequate adrenal, gonadal, and thyroid **hormone replacement**, many adults with hypopituitarism have a recognizable syndrome of weakness and diminished sense of well-being, accompanied by alterations in metabolism and body composition, as well as increased mortality. Short-term treatment with **human growth hormone** improves many of these abnormalities, but a clear improvement in functional status has yet to be demonstrated. Until such an effect is shown, the use of growth **hormone replacement** in adults with hypopituitarism remains investigational.

L3 ANSWER 32 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:242372 CAPLUS
DN 126:288316
TI The effect of low dose recombinant **human growth hormone replacement** on indices of bone remodelling and bone mineral density in hypopituitary growth hormone-deficient adults
AU Weaver, Jola U.; Monson, John P.; Noonan, Kate; Price, Christopher; Edwards, Ann; Evans, Katherine A.; James, Ian; Cunningham, John
CS Department of Endocrinology, Royal London Hospital, London, E1 1BB, UK
SO Endocrinology and Metabolism (London) (1996), 3(1), 55-61
CODEN: ENDMEM; ISSN: 1074-939X
PB Bailliere Tindall
DT Journal
LA English
TI The effect of low dose recombinant **human growth hormone replacement** on indices of bone remodelling and bone mineral density in hypopituitary growth hormone-deficient adults
IT Bone
(bone mineral d.; effect of low dose recombinant **human growth hormone replacement** on indexes of bone remodelling and bone mineral d. in hypopituitary growth hormone-deficient adults)
IT Osteocalcins
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(effect of low dose recombinant **human growth hormone replacement** on indexes of bone remodelling and bone mineral d. in hypopituitary growth hormone-deficient adults)
IT 63800-01-1, Pyridinoline 83462-55-9, Deoxypyridinoline
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(effect of low dose recombinant **human growth hormone replacement** on indexes of bone remodelling and bone mineral d. in hypopituitary growth hormone-deficient adults)

IT 9002-72-6, Growth hormone
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(recombinant human; effect of low dose recombinant **human growth hormone replacement** on indexes of bone remodelling and bone mineral d. in hypopituitary growth hormone-deficient adults)

L3 ANSWER 33 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:327780 CAPLUS
DN 122:96832
TI The effect of low dose recombinant **human growth hormone replacement** on regional fat distribution, insulin sensitivity, and cardiovascular risk factors in hypopituitary adults
AU Weaver, J. U.; Monson, J. P.; Noonan, K.; John, W. G.; Edwards, John A.; Evans, K. A.; Cunningham, J.
CS Dep. of Endocrinology, Royal London Hospital and Medical College, London, E1 1BB, UK
SO Journal of Clinical Endocrinology and Metabolism (1995), 80(1), 153-9
CODEN: JCEMAZ; ISSN: 0021-972X
PB Endocrine Society
DT Journal
LA English
TI The effect of low dose recombinant **human growth hormone replacement** on regional fat distribution, insulin sensitivity, and cardiovascular risk factors in hypopituitary adults
IT Adipose tissue
Cardiovascular system
Hypopituitarism
(low-dose recombinant **human growth hormone replacement** effect on regional fat distribution and insulin sensitivity and cardiovascular risk factors in hypopituitary human adults)
IT Lipoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Lp(a), low-dose recombinant **human growth hormone replacement** effect on regional fat distribution and insulin sensitivity and cardiovascular risk factors in hypopituitary human adults)
IT Lipoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(apo-, B, low-dose recombinant **human growth hormone replacement** effect on regional fat distribution and insulin sensitivity and cardiovascular risk factors in hypopituitary human adults)
IT 50-99-7, D Glucose, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(blood; low-dose recombinant **human growth hormone replacement** effect on regional fat distribution and insulin sensitivity and cardiovascular risk factors in hypopituitary human adults)
IT 9002-72-6, Growth hormone 9004-10-8, Insulin, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(low-dose recombinant **human growth hormone replacement** effect on regional fat distribution and insulin

sensitivity and cardiovascular risk factors in hypopituitary human adults)

IT 57-88-5, Cholesterol, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(low-dose recombinant **human growth hormone replacement** effect on regional fat distribution and insulin sensitivity and cardiovascular risk factors in hypopituitary human adults)

L3 ANSWER 34 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:927836 CAPLUS
DN 124:15423
TI Enzyme-mediated oscillatory drug release through hydrogel membranes
AU Baker, John P.; Siegel, Ronald S.
CS Schl. Pharm., Univ. California, San Francisco, CA, 94143-0446, USA
SO Materials Research Society Symposium Proceedings (1995), 394(Polymers in Medicine and Pharmacy), 119-30
CODEN: MRSPDH; ISSN: 0272-9172
PB Materials Research Society
DT Journal
LA English
AB Implantable polymeric drug-delivery devices have been constructed to deliver drugs at well-defined rates. Typically, these devices have been designed to deliver drugs at a constant rate, or in response to the concentration of a certain body metabolite. For some drugs, pulsatile delivery is sought. For example, under normal conditions, **human growth hormone** (**HGH**) is released in the body in periodic bursts. Current treatments for **HGH** deficiency often fail because **HGH** is not administered following the endogenous pattern. Thus, pulsatile **hormone-replacement** therapy should be considered. Also, it may be useful to deliver in a periodic, pulsatile manner drugs that exhibit significant acute tolerance. Currently, an oscillator is under development that is fueled by endogenous compds. and contains a variable-permeability membrane. The membrane's permeability to the substrate of an enzymic reaction is assumed to be dependent on the concentration of the product of the reaction in a manner that displays product inhibition. Under certain conditions, this neg.-feedback control can lead to oscillations in the membrane's permeability to substrate. If the membrane's permeability to a drug is simultaneously affected, then this will lead to oscillatory drug release. We report encouraging initial studies. A simple theor. model has been developed for the membrane oscillator, and results of simulations based on the model are discussed. Diffusion-cell studies have been performed with a variable-permeability poly(N-isopropyl-acrylamide-co-methacrylic acid) hydrogel membrane. Using glucose as a probe solute, the results show that lowering the pH induces hydrogel volume collapse and cessation of glucose permeation across the membrane.

L3 ANSWER 35 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:353958 CAPLUS
DN 122:123562
TI Treatment of growth hormone-deficient adults with recombinant human growth hormone increases the concentration of growth hormone in the cerebrospinal fluid and affects neurotransmitters
AU Johansson, Jan-Ove; Larson, Goran; Anderson, Mats; Elmgren, Anders; Hynsjo, Lars; Lindahl, Anders; Lundberg, Per-Arne; Isaksson, Olle GP; Lindstedt, Sven; Bengtsson, Bengt-Ake
CS Departments of Internal Medicine, Clinical Chemistry and Neurology, University of Goteborg, Goteborg, Swed.
SO Neuroendocrinology (1995), 61(1), 57-66

CODEN: NUNDAJ; ISSN: 0028-3835
PB Karger
DT Journal
LA English
AB In a double-blind, placebo-controlled trial, the effects of recombinant **human growth hormone** were studied on cerebrospinal fluid concns. of growth hormone, insulin-like growth factor 1 (IGF-1), insulin-like growth factor binding protein-3 (IGFBP-3), monoamine metabolites, neuropeptides and endogenous opioid peptides. Twenty patients, 10 patients in each of 2 groups, with adult-onset, growth hormone deficiency were treated for 1 mo with recombinant **human growth hormone** (0.25 U/kg/wk) or placebo. All the patients received the appropriate thyroid, adrenal and gonadal **hormone replacement**. In cerebrospinal fluid, the mean concentration of growth hormone increased from 13.3 to 149.3 μU/L, during recombinant **human growth hormone** treatment. The cerebrospinal fluid IGF-1 concentration increased from 0.67 to 0.99 μg/L and the IGFBP-3 concentration rose from 13.4 to 17.5 μg/L. The dopamine metabolite homovanillic acid decreased from 282.1 to 234.3 nmol/L and the vasoactive intestinal peptide decreased from 4.1 to 3.7 pmol/L. Cerebrospinal fluid immunoreactive β-endorphin increased from 24.4 to 29.9 pmol/L. There were no significant changes compared to baseline in the cerebrospinal fluid concns. of enkephalins, dynorphin A, the norepinephrine metabolite 3-methoxy-4-hydroxyphenyl-ethyleneglycol, the serotonin metabolite 5-hydroxyindoleacetic acid, γ-aminobutyric acid, somatostatin or ACTH-releasing factor. The authors conclude that treatment with recombinant **human growth hormone** causes a tenfold increase in growth hormone in the cerebrospinal fluid, thereby indicating that recombinant **human growth hormone** passes the blood-cerebrospinal fluid barrier. The cerebrospinal fluid concns. of IGF-1 and IGFBP-3 increased significantly. Simultaneously, the cerebrospinal fluid concns. of homovanillic acid and vasoactive intestinal peptide decreased and the concentration of β-endorphin immunoreactivities increased significantly. These changes might explain the improved quality-of-life in patients with growth hormone deficiency following replacement therapy with growth hormone.

L3 ANSWER 36 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:622383 CAPLUS
DN 121:222383
TI Ultrastructure of cementogenesis as affected by growth hormone in the molar periodontium of the hypophysectomized rat
AU Clayden, A. M.; Young, W. G.; Zhang, C. Z.; Harbrow, D.; Romaniuk, K.; Waters, M. J.
CS Faculty of Dentistry, University of Queensland, 4072, Australia
SO Journal of Periodontal Research (1994), 29(4), 266-75
CODEN: JPDRAY; ISSN: 0022-3484
DT Journal
LA English
AB To document the effect of hypophysectomy and growth **hormone replacement** on the ultrastructure of cementogenesis in the developing rat 3rd molar, 12 female Wistar rats were randomly allocated to normal control, hypophysectomized or hypophysectomized plus **human growth hormone** (for 10 days) treatment groups. The results of this study by electron and light microscopy and morphometry have shown that qual. and quant. changes occur in the organelles of cementoblasts forming cellular cementum as a result of hypophysectomy and growth **hormone replacement**. After hypophysectomy, the changes of less prominent nucleoli and nuclear pores, less prominent Golgi apparatuses and decreased endoplasmic reticulum can be interpreted as diminished cementum matrix biosynthesis - an interpretation that can be

confirmed morphometrically by less cellular cementum formation. Growth **hormone replacement** for 10 days reactivates protein synthesis and cementogenesis as evidenced by ultrastructural changes in cementoblasts and a greater production of cementum.

L3 ANSWER 37 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:622376 CAPLUS
DN 121:222376
TI Impaired cardiac performance in GH-deficient adults and its improvement after GH replacement
AU Cittadini, Antonio; Cuocolo, Alberto; Merola, Bartolomeo; Fazio, Serafino; Sabatini, Domenico; Nicolai, Emanuele; Colao, Annamaria; Longobardi, Salvatore; Lombardi, Gaetano; Sacca, Luigi
CS Med. Sch., Federico II Univ., Naples, 80131, Italy
SO American Journal of Physiology (1994), 267(2, Pt. 1), E219-E225
CODEN: AJPHAP; ISSN: 0002-9513
DT Journal
LA English
IT Heart
(performance of, impairment of, in growth hormone-deficient **human, growth hormone replacement** therapy effect on)

L3 ANSWER 38 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:646717 CAPLUS
DN 121:246717
TI Beneficial effects of 12 months replacement therapy with recombinant human growth hormone to growth hormone deficient adults
AU Rosen, Thord; Johannsson, Gudmundur; Hallgren, Per; Caidahl, Kenneth; Bosaeus, Ingvar; Bengtsson, Bengt-Aake
CS Research Centre for Endocrinology and Metabolism, Sahlgrenska Hospital, Goeteborg, Swed.
SO Endocrinology and Metabolism (London) (1994), 1(1), 55-66
CODEN: ENDMEM; ISSN: 1074-939X
DT Journal
LA English
IT Bone
Lung
(recombinant **human growth hormone replacement** therapy to growth hormone deficient adults)
IT Osteocalcins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(recombinant **human growth hormone replacement** therapy to growth hormone deficient adults)
IT Glycoproteins, specific or class
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(IGF-BP-3 (insulin-like growth factor-binding protein 3), recombinant **human growth hormone replacement** therapy to growth hormone deficient adults)
IT Lipoproteins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(high-d., recombinant **human growth hormone replacement** therapy to growth hormone deficient adults)
IT Collagens, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pro-, type III, recombinant **human growth hormone replacement** therapy to growth hormone deficient adults)

IT 9002-72-6, Growth hormone
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(recombinant **human growth hormone** **replacement** therapy to growth hormone deficient adults)
IT 57-88-5, Cholesterol, biological studies 7440-70-2, Calcium, biological studies 9004-10-8, Insulin, biological studies 67763-96-6, IGF-I
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(recombinant **human growth hormone** **replacement** therapy to growth hormone deficient adults)

L3 ANSWER 39 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:623566 CAPLUS
DN 115:223566
TI **Human growth hormone replacement** therapy: pharmacological and clinical aspects
AU Lunde Joergensen, Jens Otto
CS Med. Dep. M, Aarhus Kommunehosp., Aarhus, Den.
SO Endocrine Reviews (1991), 12(3), 189-207
CODEN: ERVIDP; ISSN: 0163-769X
DT Journal; General Review
LA English
TI **Human growth hormone replacement** therapy: pharmacological and clinical aspects

L3 ANSWER 40 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:585388 CAPLUS
DN 113:185388
TI The Seville **hGH** Symposium. Clinical Aspects of Growth **Hormone Replacement** Therapy. Proceedings of the **hGH** Symposium Seville, Spain, April 18-21, 1990. [In: Hormone Res., 1990; 32(Supply 4)]
AU Girard, J.; Christiansen, J. S.; Editors
CS Switz.
SO (1990) Publisher: (Karger, Basel, Switz.), 105 pp.
DT Book
LA English
TI The Seville **hGH** Symposium. Clinical Aspects of Growth **Hormone Replacement** Therapy. Proceedings of the **hGH** Symposium Seville, Spain, April 18-21, 1990. [In: Hormone Res., 1990; 32(Supply 4)]

L3 ANSWER 41 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1983:569991 CAPLUS
DN 99:169991
TI Human growth hormone increases intestinal vitamin D-dependent calcium-binding protein in hypophysectomized rats
AU Elizabeth, M.; Bruns, H.; Vollmer, Sheila S.; Bruns, David E.; Overpeck, James G.
CS Med. Sch., Univ. Virginia, Charlottesville, VA, 22908, USA
SO Endocrinology (1983), 113(4), 1387-92
CODEN: ENDOAO; ISSN: 0013-7227
DT Journal
LA English
AB The effects were studied of hypophysectomy and pituitary **hormone** **replacement** on vitamin D [1406-16-2]-dependent Ca-binding protein (CaBP) in rat small intestine. The concentration of immunoreactive CaBP per mg intestinal protein was decreased by at least 56% in hypophysectomized rats compared to intact pair-fed controls. Alkaline phosphatase and total protein also were reduced by hypophysectomy, but pair-feeding produced comparable decreases. Daily injections of 2, 10, or 50 μg **human**

growth hormone (**hGH**) [9002-72-6] for 9 days produced a dose-dependent increase in CaBP. At the highest **hGH** dose (50 μg), the content of CaBP was increased 2-4-fold to intact levels. By comparison, the increases in total protein and alkaline phosphatase were small (25-40% and 80-90%, resp.). The induction of CaBP preceded the other protein responses; half-maximal increases in CaBP occurred after 2 days of **hGH** (50 μg/day) treatment before statistically significant changes in total protein or alkaline phosphatase activity. **HGH** was the most potent pituitary hormone tested; ovine TSH [9002-71-5] (25 milliunits/day) had no effect on CaBP, and ovine prolactin [9002-62-4] (10 or 50 μg/day) increased CaBP by only 25-27%. Thus, the vitamin D-dependent intestinal CaBP in hypophysectomized rats is regulated by GH; the pituitary may be involved in regulating vitamin D-dependent intestinal adaptations.

L3 ANSWER 42 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1980:16233 CAPLUS
DN 92:16233
TI The effect of **human growth hormone replacement** on parathyroid function and vitamin D metabolism
AU Gertner, J. M.; Horst, R. L.; Rasmussen, H.
CS Sch. Med., Yale Univ., New Haven, CT, 06510, USA
SO Proceedings of the Workshop on Vitamin D (1979), 4th(Vitam. D: Basic Res. Its Clin. Appl.), 265-6
CODEN: PWVDDU; ISSN: 0721-7110
DT Journal
LA English
TI The effect of **human growth hormone replacement** on parathyroid function and vitamin D metabolism

L3 ANSWER 43 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1978:167970 CAPLUS
DN 88:167970
TI Role of growth hormone in the regulation of aldosterone biosynthesis
AU McCaa, Robert E.; Montalvo, Jose M.; McCaa, Connie S.
CS Dep. Physiol. Biophys., Univ. Mississippi Sch. Med., Jackson, MS, USA
SO Journal of Clinical Endocrinology and Metabolism (1978), 46(2), 247-53
CODEN: JCEMAZ; ISSN: 0021-972X
DT Journal
LA English
AB The role of somatotropin in the regulation of aldosterone biosynthesis in human beings was studied. The aldosterone response to ACTH was determined in 8 normal human beings before and after dietary Na restriction and compared with the aldosterone response observed in 3 patients with panhypopituitarism and 3 patients with isolated GH deficiency. Plasma aldosterone concentration, plasma cortisol concentration, and plasma renin activity were determined by radioimmunoassay. A normal aldosterone, cortisol, and renin response to dietary Na restriction and ACTH was observed in the subjects with isolated GH deficiency. Plasma aldosterone concentration was normal under resting conditions in the patients with panhypopituitarism, but failed to increase in response to ACTH or Na deprivation. A normal response of plasma renin activity to Na deprivation was observed in the subjects with panhypopituitarism. A marked increase in the sensitivity of the adrenal glomerulosa to ACTH was observed in normal subjects and in subjects with isolated GH deficiency and panhypopituitarism during Na deficiency. The subjects with isolated GH deficiency and panhypopituitarism were maintained on **hGH** replacement therapy for 12 mo. All 6 subjects showed an increased growth rate, but GH replacement therapy failed to restore a normal aldosterone response to ACTH or Na deprivation in the subjects with panhypopituitarism. Somatotropin is not the essential pituitary hormone required for a normal aldosterone response to ACTH or Na

deprivation since a normal aldosterone response was observed in subjects with isolated GH deficiency, and growth **hormone replacement** therapy failed to restore a normal aldosterone response in the subjects with panhypopituitarism.

L3 ANSWER 44 OF 44 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1974:23020 CAPLUS
DN 80:23020
TI Effect of **HGH** [**human growth hormone**] **replacement** therapy on concentration of 15 serum proteins
AU Clarke, H. G. Minchin; Grant, D. B.; Putman, D.
CS Clin. Res. Cent., Harrow/Middlesex, UK
SO Archives of Disease in Childhood (1973), 48(8), 608-11
CODEN: ADCHAK; ISSN: 0003-9888
DT Journal
LA English
TI Effect of **HGH** [**human growth hormone**] **replacement** therapy on concentration of 15 serum proteins